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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/374,586	08/13/1999	DAVID J. PINSKY	59167/JPW/JM	3944

7590 08/18/2003

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EXAMINER
CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
1632	24

DATE MAILED: 08/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

24

Office Action Summary	Application No.	Applicant(s)	
	09/374,586	PINSKY, DAVID J.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2003 and 13 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7,9-13,17-19,22-24,27 and 39-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *39 and 42-46* is/are allowed.

6)☐ Claim(s) *1, 2, 7, 9-13, 17-19, 22-24 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' amendments filed 5-12-03 and 6-13-03 have been entered. Claims 3-6, 8, 16, 20 and 21 have been canceled. Claims 1, 2, 7, 9-13, 17, 19, 22-24 and 27 have been amended. Claims 28-38 have been added. Claims 34-38 have been canceled. Claims 39-46 have been added. Claims 1, 2, 7, 9-13, 17-19, 22-24, 27 and 39-46 are pending and under consideration.

Claim Objections

1. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

The amendment filed 5-12-03 added claims 28-38 but only claims 34-38 are shown in the text followed. However, in the marked version (unofficial) of the amended claims, claims 28-38 are shown. The amendment filed 6-13-03 indicates that new claims 34-38 were mistakenly referred to as new claims 28-38 and the new claims 34-38 have been canceled, and the pending claims are 1, 2, 7, 9-13, 17-19, 22-24, 27 and 39-46. Therefore, claims 28-33, which apparently are duplicates of claims 39-44, will not be considered pending claims in the present Official action. Cancellation of claims 28-33 is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 17-19 and 22-24 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and is repeated for the reasons set forth in the preceding Official action mailed 11-7-02 (Paper No. 21). Applicant's arguments filed 5-12-03 and 6-13-03 have been fully considered but they are not persuasive.

Applicants cite specification page 14, lines 19-32, page 23, lines 7-15, page 27, lines 19-31, and page 29, lines 34 to page 30, line 7 and argue that when read together the specification has support for a method of determining whether a compound increase incidence of ICH with or without the presence of said compound (amendment, p. 9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 11-7-02 (Paper No. 21). The specification page 23, lines 7-15, page 27, lines 19-31, and page 29, lines 34 to page 30, line 7 disclose ICH assay and compare the effect of CD39 and aspirin on the incidence of ICH but fail to provide support for comparing the incidence of ICH with or without the presence of CD39. Further, there is no nexus between no increase of the incidence of ICH and capability of a compound of treating or preventing the thrombotic or ischemic disorder in a subject. Thus, claims 17-19 and 22-24 remain rejected under 35 U.S.C. 112 first paragraph.

4. Claims 1, 2, 7, 9-13 and 27 remain rejected and claims 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of soluble CD39 in the treatment and prevention of thrombotic and ischemic disorders in mice and BIBU52 in rhesus and marmoset monkeys (Guth et al., abstract), does not reasonably provide enablement for the use of an active fragment of CD39 comprising amino acid 1-50 of SEQ ID No. 2 or about 20-80 amino acid of SEQ ID No. 1 that mimics the active site, or for the use of any deletion mutant, insertion mutant, or any truncated mutant of CD39 polypeptide for treating or preventing stroke in a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 11-7-02 (Paper No. 21). Applicant's arguments filed 5-12-03 and 6-13-03 have been fully considered but they are not persuasive.

Claims 40 and 41 are directed to a method for treating or preventing stroke in a human subject by using a deletion mutant of the CD39 polypeptide, comprising amino acid sequence of SEQ ID No. 2, which lacks a transmembrane domain (TMD), or a CD39 polypeptide comprising amino acids 1-50 of SEQ ID No. 2.

Applicants argue that the teachings of Schutle et al. are not relevant to the claimed invention because the claims do not recite using a CD39 variant containing a FLAG-tag or a GPI anchor and synthesizing polypeptide fragment and identification of therapeutic fragment do not require undue experimentation (amendment, p. 14). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 11-7-02 (Paper No. 21). Schutle teaches that apyrase conserved regions (ACR)-1, -4, and -5 within CD39 polypeptide are required for

maintenance of biochemical activity of the CD39 polypeptide (e.g. abstract). Therefore, a CD39 polypeptide mutant must comprise ACR-1, -4, and -5 in order to maintain its biochemical activity so as to treat or prevent stroke in mice or a subject. The claims encompass using CD39 polypeptide **comprising** amino acid 1-50 of SEQ ID No. 2 or about 20-80 amino acid of SEQ ID No. 1 that mimics the active site, or any deletion mutant, such as deletion of TMD, insertion mutant, or any truncated mutant of CD39 polypeptide for treating or preventing stroke in a subject. The term "comprising" is an open language term and means adding any amino acid sequence, including FLAG-tag or GPI anchor, onto 5' and/or 3' end of the core amino acid sequence. Further, the presence of FLAG-tag is to ensure membrane expression of the protein and does not seem to interfere the biological activity of CD39 polypeptide. Thus, the teachings of Schutle is relevant to the claimed invention.

As discussed in the preceding Official action mailed 11-7-02 (Paper No. 21), amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Although method of synthesizing polypeptide fragment was known, but protein function was unpredictable from mere amino acid sequence at the time of the invention, therefore, it would require undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention claimed.

Conclusion

Claims 1, 2, 7, 9-13, 17-19, 22-24, 27, 40 and 41 are rejected. Claims 39 and 42-46 are in condition for allowance.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

SLC